Delaying cancer cases in Urology during COVID-19: review of the literature.

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Abstract

Purpose: Coronavirus Disease 2019 (COVID-19) is a global pandemic affecting hospital systems and the availability of resources for surgical procedures. Our aim is to provide guidance for urologists to help prioritize urologic cancer surgeries.

Material and Methods: We reviewed published literature on bladder cancer, upper tract urothelial carcinoma (UTUC), penile cancer, testis cancer, prostate cancer, renal cancer, and adrenal cancer.

Results: For muscle invasive bladder cancer (MIBC), delays should be less than roughly 10 weeks and neoadjuvant chemotherapy should be considered. For non-MIBC, patients should be counseled appropriately based on risk and intravesical therapies can continue. UTUC should also be treated with minimal delays for high risk patients, especially with ureteral tumors. Surgery for T1 renal cancers when indicated can be delayed until adequate resources are available. Patients with T2 renal cancer should be considered for early surgery if there are unfavorable pre-operative characteristics. Higher stage renal tumors should be considered for early surgery. Early multi-disciplinary approach is recommended for metastatic renal cancers. High risk prostate cancer may need preferential treatment and consideration of neoadjuvant hormonal therapy. Penile cancer can have worse sexual or oncologic outcome with prolonged surgical delay. Likewise, adrenal cancer is aggressive and needs early surgical treatment. Testicular cancer should be treated in a timely manner with surgery or chemotherapy, as indicated.

Conclusions: This review should further assist urologists in recognizing patients with potentially aggressive tumor biology that warrant early treatment.

Introduction

Severe acute respiratory syndrome coronavirus – 2 (SARS-CoV-2) can induce a severe respiratory compromise with rapid human-to-human transmission stressing entire hospital systems. In order to conserve resources and prevent further spread of COVID-19, the CDC and hospital systems have requested physicians to reconsider non-urgent procedures. Here, we aim to discuss the effect of COVID-19 on urologic cancers, specifically regarding anticipated delays in surgical treatment.

Background

COVID-19 is highly transmissible and can cause respiratory issues requiring ventilation, ICU care, and death. Epidemiologic factors and high rates of hospitalization for patients with COVID-19 have resulted in widespread cancellation of elective surgical procedures in favor of prioritizing urgent procedures.

In response to COVID-19, recommendations for prioritizing cases have been published[1]. With reopening of operating rooms, region-specific factors should guide treatment as resources and COVID-19 surges vary across the world. Throughout this process, urologists should assist in appropriate timing of treating urologic cancers. Thus, our aim is to provide further guidance by demonstrating the potential biases in the literature and add to published recommendations. Tumor biology may dictate treatment that deviates from these recommendations and should be discussed with patients.

Bladder Cancer

Several publications have discussed potential consequences in delaying extirpative surgery for muscle invasive bladder cancer (MIBC). Boeri et al. studied their cohort of MIBC patients (cT2-T4) and found that a delay greater than 10 weeks after the last neoadjuvant chemotherapy (NAC) cycle led to worse outcomes for cancer-specific and overall mortality. Delays in surgery increased mortality even when accounting for age, gender, and extent of disease[2]. Similarly, in patients that only underwent radical cystectomy without NAC, Sanchez-Ortiz et al. found that even after adjusting for pathologic aggressiveness, patients who were delayed longer than 12 weeks had worse survival – 3-year estimated survival for the delayed group was 34.9%±13.5% compared to 62.1%±4.5% for patients receiving surgery before 12 weeks[3]. Other groups had similar findings that a delay in surgery led to worse outcomes when greater than 90 days passed from diagnosis or NAC to surgery[4].

Despite these studies suggesting the importance of performing cystectomy in a timely manner, Alva et al. demonstrated that there was no survival benefit to earlier cystectomy (<10 weeks after last dose of NAC)[5]. The study also found no difference between groups of patients that were delayed 12 weeks, but 10 weeks was used as a cut off to add confidence to their conclusions. This group found that pathologic stage was a factor in overall survival but could not find that actual timing of radical cystectomy played a role in survival outcomes. Park et al. also published a retrospective review that found no significantly detrimental impact to delaying surgery until 28 weeks after the TURBT diagnosis[6]. Furthermore, a 6-week delay in NAC initiation or a 22-week delay from NAC initiation to RC did not affect survival (about 10-12 weeks from NAC completion to RC). This group found that inferior outcomes were related to the

presence of extravesical disease. In patients that did not undergo NAC, Nielsen et al. also found that interval from diagnosis to radical cystectomy of 3 months was not necessarily associated with progression and worse survival outcomes[7].

Patients with variant histology on final surgical pathology after cystectomy, and patients experiencing an 8 week delay had worse overall survival[8]. Within the same study, however, patients with clinical variants (diagnosed at TURBT) had 12 weeks as the cutoff for survival differences. This study did not specify any differences between variant histology.

NAC should be carefully discussed with patients by their medical oncologist as there may be associated risks with exposure and decreased immunity to COVID-19. Audenet et al. found that delays from time of TURBT to NAC by more than 8 weeks, without delay from NAC to radical cystectomy, can affect the disease course[9]. After a median follow up time of 45.7 months, no significant changes in overall survival were noted, but patients that had a delay to NAC were more likely to be upstaged on final surgical pathology. RFS or CSS were not calculated in this study.

For diagnosing bladder cancer, Wallace et al. found that delays occur between onset of symptoms and diagnosis. This study divided delay times between onset of symptoms to general practitioner (GP), GP to specialist, and then time to the OR. The delay from onset of symptoms to GP greater than 14 days played a significant role in survival outcomes because these patients consequently had higher stage tumors and worse survival outcomes of 5% at 5 years compared to those that did not have any delay[10]. During this pandemic, patients likely will experience a delay in seeing a GP due to widely issued stay-at-home orders. This stresses the importance of

continuing to perform screening cystoscopy, during the pandemic, for patients suspected to have bladder cancer in order to accurately identify the aggressiveness of disease.

For NMIBC, the literature is limited for the effects of delaying intravesical therapy. However, studies have compared early versus late cystectomy for high risk NMIBC patients and have found that prolonged delays can affect survival. Jager et al. studied effects on delayed cystectomy for high risk NMIBC and found that patients that were delayed for ≥ 13 months may start to see an effect on CSS[11]. The survival outcomes for aggressive NMIBC is likely dependent on the tumor biology rather than specific timing delays. Hautmann et al. studied specifically T1 G3, high risk disease and found that CSS was 83.9% vs 74.8% at 5 years and at 10 years 78.9% versus 64.5% in favor of immediate cystectomy (within 90 days) compared to deferred cystectomy (second TURBT, BCG administration and repeat TURBT), which is likely result of the lack of response to therapy[12]. And for patients with initial response to intravesical therapy by looking at patients that had recurrent NMIBC disease, patients that received one additional salvage intravesical treatment were able to retain their bladder for 1.7 years longer without any survival detriment[13]. Results with deferred cystectomy is highly variable due to the differences in tumor biology and responsiveness to intravesical therapy and it is hard to generalize for the purposes of this review. For high-risk NMIBC that are considering cystectomy, delays experienced due to the COVID-19 pandemic should pose minimal risk to survival outcomes, but urologists should still carefully assess the aggressiveness of each patient's individual cancer to determine appropriate timing of cystectomy.

For NMIBC, patients requiring intravesical therapy, especially induction dose, for intermediate or high-risk NMIBC should still be considered with the clear benefits of intravesical therapy.

Discussion: A systematic review and meta-analysis discussing potential delays in treating MIBC ultimately found that an acceptable length of delay could not be determined, but recognized that delays do cause a detrimental effect on overall survival[4]. Based on these past studies, patients with MIBC should consider NAC and should undergo radical cystectomy within 10-12 weeks either after TURBT without NAC or after NAC completion. However, as many of these studies demonstrated issues with delaying surgery in terms of disease progression, MIBC especially those that are extravesical may be prioritized. For new patients, surveillance cystoscopy to assess risk and burden of disease is still important and should continue during this pandemic (Table 1). Finally, the literature on delaying intravesical therapy in lacking, but they should continue with proper counseling.

Upper Tract Urothelial Cancer (UTUC)

Literature review of UTUC demonstrated that delay in surgical time likely does affect overall survival outcomes in higher risk cases. Lee et al. found that surgical delay of greater than 1 month was not an independent prognostic factor when all 138 patients with upper tract urothelial carcinoma were included in their survival curves[14]. However, once the analysis was further sub-categorized by location to renal pelvic tumor and ureteral tumors, tumors in the ureter had worse prognosis for patients that delayed surgery by one month -CSS (87.9% vs 54.5%) and RFS (85.6% vs 60.7%). Of note, both low-grade and high-grade urothelial carcinoma were included in their analysis. A study done by Waldert et al. found that a 3 month delay to

radical nephroureterectomy (RNU) may not necessarily have worse survival outcomes at 3 and 5 years[15]. This study treated delay time as a continuous variable as well and found that longer time to surgery was correlated with advancing pathologic stage, higher tumor grade, concomitant CIS, tumor necrosis, infiltration, worse CSS, and increased likelihood of recurrence. This study performed a subgroup analysis with muscle invasive disease (≥ pT2), which demonstrated that there was no significant difference in survival outcomes (RFS and CSS) using 3 months as a cutoff point. However, once again they noted that these muscle invasive patients experiencing a delay in surgery had worsening surgical pathology (advanced stage, higher grade, infiltrative tumor architecture, and lymphovascular invasion). Nison et al. also found similar findings with no significant difference with survival outcomes CSS, RFS, and metastasis free survival (MFS) in a muscle invasive subgroup. Their group compared patients that had median time of 62 days compared to 47 days until RNU[16]. Sundi et al. studied the consequences of a 3-month delay prior to RNU and did not find any negative effect with respect to RFS, DSS, and OS. Patients in this cohort had approximately 79% high risk patients. Even after excluding patients from the delayed group that had undergone NAC, there was no decrement in 5- year DSS (71.6% vs 81.5%) and OS (61.3% vs 77%) among those waiting longer than 3 months. In this secondary analysis, of the delayed group (54 patients) – 27 had NAC and 9 more patients were delayed from being on surveillance and endoscopic management, meaning that a portion of patients that were delayed likely had lower risk disease[17].

Discussion: It has been well established that low grade UTUC is less aggressive and safe to keep on surveillance and undergo endoscopic management. Until burden and risk of disease is determined, similarly to bladder cancer, patients should undergo thorough evaluation with endoscopy. In evaluating these studies, patients with high-risk disease may be preferentially

treated as many studies were retrospective and preferentially treated aggressive patients sooner (<3 months). Patient with tumor location in the ureter may also require limited delay (Table 1). While some studies have shown efficacy with NAC and could delay surgery, those patients in whom immunosuppression is of concern, adjuvant therapy after early surgery may be offered with success[18].

Renal Cancer

For small renal masses (≤ 4 cm), active surveillance has become an acceptable standard of care. These patients are typically followed to monitor growth kinetics to determine intervention, and typical follow-up during active surveillance was in 6-month to 12-month intervals. Uzosike et al. noted in their evaluation of patients in the Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) trial that no patients on active surveillance died from kidney cancer or developed metastatic disease[19]. Other studies looking at the SEER database have found a small rate (<4%) of metastasis for masses <5cm[20].

For larger renal masses (≥ 4cm), Mano et al. evaluated data from 1,278 patients in a retrospective analysis of which 267 (21%) patients had surgical wait times (SWT) greater than 3 months. Median mass size was 6.2 cm (6.5 cm for SWT ≤ 3 mo. and 5.7 cm for SWT > 3 mo.)[21]. On analysis, SWT were not associated with disease upstaging, recurrence, or cancer specific survival. Stec et al. also retrospectively analyzed a cohort of patients with a mean renal mass size of 6.4 ± 4.4 cm. and found no differences in overall survival (OS), cancer-specific survival (CSS), or recurrence-free survival (RFS) when delaying surgery for patients and accounting for differences in tumor grade and pathology[22]. Their group found that 5-year OS, CSS, or RFS was determined based on the staging of disease, histology, tumor grade, and extent of spread at

presentation. RFS was found to be worse in patients who underwent surgery within a month likely because larger, more aggressive-appearing masses were preferentially treated. In a study by Kim et al., similar findings were shown in a retrospective review of 1,732 patients who underwent surgery for RCC for masses with a mean size of 8.9±2.6 cm that were at least stage T2a[23]. Their group found that SWT of 1-3 months compared to SWT of <1 month was not an independent predictor of pathological upstaging, RFS, or CSS. This study also discussed the impact of SWT on symptomatic patients as they had higher clinical and pathologic stages, but there was no association between SWT and pathologic upstaging, CSS, or RFS. Considering the literature, these studies were retrospective in nature and clinicians appeared to selectively and more urgently operate on patients with more aggressive-appearing renal tumors. Also with symptomatic patients, Lee et al. found that patients with flank pain, hematuria, varicocele, constitutional symptoms correlated to aggressive histology and worse survival outcomes[24]. DSS was 91% at 5 years for non-symptomatic patients versus 68% at 5 year for symptomatic patients. Thus, RCC (≥T2) can be further risk-stratified to determine urgency of treatment. To assist in predicting which renal masses are more aggressive, nomograms can help predict high-risk, high-grade pathology that requires more urgent attention[25]. Renal mass biopsy may provide some benefit, clear cell RCC, papillary RCC, and chromophobe typically correctly identify the pathology, however Fuhrman grade is less concordant. Abel et al. also studied concordance for high risk pathological features and found that 31.7% of patients had the same Fuhrman grade as final path and 67.9% had same concordance if stratified by low and high risk[26] .

Metastatic renal cell carcinoma that is under consideration for cytoreductive nephrectomy (CN) should consider neoadjuvant therapy based on early results. Deferring immediate CN may not cause any harm in survival outcomes based on the SURTIME and CARMENA trials[27, 28].

The SURTIME trial accrued fewer patients than the CARMENA trial, but demonstrated that there was no significant difference in survival for patients that deferred CN compared to patients that underwent upfront CN[27]. Of the 48 patients that deferred CN, 14 patients went against protocol and 6 underwent surgery. When these off-protocol patients were studied, the deferred CN patients seemed to have improved overall survival. There still appears to be some role in CN, especially in those patients that have some response to neoadjuvant immunotherapy which can also help to delay surgery. For more localized renal cell carcinomas, Rini et al. also demonstrated that Pazopanib can be administered for 8-16 weeks prior to surgery to decrease tumor size in a Phase II trial (92% of patients)[29].

Discussion: Patients with renal masses (≥T2) should undergo careful evaluation, as these patients still carry a risk for metastasis. These studies looking at delaying surgery are retrospective and patients with high-risk features typically had operations without significant delay, which may account for the similar survival outcomes. Priority should be given to those with aggressive features– imaging findings, possible renal mass biopsy results, symptoms etc. (Table 1). For those with metastatic kidney cancer, neoadjuvant options should be discussed with medical oncologists for immune risks with COVID-19.

Prostate Cancer

Delaying radical prostatectomy (RP) for prostate cancer depends heavily on the clinical staging. Meunier et al. published a retrospective analysis of 513 patients by selecting biochemical recurrence (BCR) as the primary endpoint[30]. The study found that for surgical delay, there was no threshold for patients with Gleason 6 (3+3), a 90-day threshold for Gleason 7, and a 60-day threshold for Gleason ≥ 8 cancers. Other studies using biochemical recurrence as the

endpoint, found 3 months to 6 months as a cut-off point[31, 32]. Similar findings were found for patients considering radiation therapy, where patients had a higher likelihood of PSA failure for patients with high risk disease after a 2.5 month period, which is similar to the outcomes for surgical delay[33].

Other studies have suggested that it is possible to delay surgery for longer periods of time. Recently, Ginsburg et al. performed a retrospective review of the National Cancer Database and found that delays up to 12 months did not have worse oncological outcomes (adverse pathology, upstaging on RP, or secondary treatment) for intermediate and high-risk prostate cancer[34]. Gupta et al. did not find any significant differences in adverse pathologic outcomes or BCR or MFS comparing those treated within 3 month to those waiting 3-6 months[35]. Gleason Group 5 patients primarily underwent RP at <3 mo. (87%). Patel et al also found 6 months to be an acceptable delay, but acknowledges that to evaluate the data, Grade Group 3,4,and 5 were included together as high-risk patients[36]. Fossati et al. studied 2,653 patients that had undergone RP and found that 283 patients experienced BCR and 84 patients developed clinical recurrence (CR)[37]. Furthermore, patients with highest risk started to experience higher rates of BCR and CR after 12 months of surgical treatment delay. Similarly, most high-risk patients were treated within 12 months (386 patients) and 208 patients were treated within 3 months. Only a total of 17 patients were treated after 12 months delay.

The role of neoadjuvant therapies may play a role in higher risk prostate cancer. A randomized study for neoadjuvant hormonal therapy (NHT) demonstrated that patients undergoing 12 weeks of cyproterone acetate tended to have prostatectomy specimens with lesser weights, smaller tumor volumes, and greater Gleason scores. There were significantly fewer

positive margin rates in patients undergoing NHT (27.7% vs. 64.8%, p<0.01). Interestingly, treated patients had higher rates of seminal vesicle involvement (27.7% vs 14.3%, P<0.05)[38]. Patients followed for 36 months showed no difference between the two groups in terms of biochemical progression, and at long-term follow up (median time 6 years), there was a biochemical recurrence-free survival benefit in patients with initial PSA greater than 20ng/ml that had received NHT[38]. Another long-term study followed 354 patients who received Goserelin and Flutamide for 3 months[39]. In the initial studies, patients undergoing NHT demonstrated improved pathological outcomes after RP. These patients were then followed over 4 years, and patients with cT2 tumors showed lower local recurrence rates in patients undergoing NHT. However, this finding was not present in the cT3 group. Although there were fewer positive margin rates in the initial study, the NHT cohort did not necessarily translate to better PSA progression rates after 4 years of follow up[39]. Of note, Meyer et al. did find that patients receiving more than 3 months of NHT prior to RP had a lower risk of PSA failure compared to patients receiving only surgery without NHT at the 5-year mark[40].

Lastly, recent studies have compared patients neoadjuvant chemohormonal therapy (NCHT) with RP to high risk (>cT3a, Gleason 8-10, PSA > 50ng/ml, or pelvic metastatic involvement) patients only undergoing RP or RP with NCHT. Patients receiving NCHT (docetaxel-based) combined with RP were more likely to achieve undetectable postoperative PSA as well as more favorable surgical pathology with organ confined disease and less pT3 or pT4 disease[41]. Biochemical recurrence also occurred earlier in the untreated group (9 months vs 13 months biochemical PFS). In the latest CALGB 90203 Phase III randomized study of patients undergoing NCHT and RP to patients having RP alone, the NCHT group had lower pathologic T-stage, lower likelihood of seminal vesicle invasion, positive lymph nodes, or positive surgical

margins[42].The survival outcome remains to be studied. It remains important to note that treatment with NCHT is associated with adverse side effects such as immunosuppression.

Discussion: For prostate cancer, the literature provides significant variability in safe delay times. Some found delays of 60 days can affect recurrence free survival, whereas other studies found no survival outcome differences up to 12 months. Studies finding that longer delays were feasible may be the fact that most high-risk patients were treated within 3 months. Studies have also demonstrated that a 3-month course of NHT does not negatively impact long-term survival and would allow patients to safely delay surgery. We recommend consideration of neoadjuvant therapy in high-risk patients that may have prolonged delay (Table 1). In terms of diagnosing prostate cancer, patients with higher risk of prostate cancer based on PSA, age, physical exam and other adjunctive screens should preferentially be biopsied.

Adrenal Cancer

Adrenocortical Carcinoma (ACC) is an aggressive malignancy, the median disease specific survival (DSS) of ACC is 34 months and 5-year DSS is 39% from a study of patients with localized primary disease[43]. Meyer et al. followed 20 patients that underwent operative treatment for adrenal cortical carcinoma[44]. From this cohort, Stage I and II had mean survival for 65 months compared to Stage III which was 38 months and Stage IV which was 19 months. The 5-year survival rate was 23%. Neoadjuvant therapy for adrenocortical carcinoma demonstrating significant differences in clinical outcomes is lacking. Adrenocortical carcinoma is an aggressive disease that needs complete surgical resection, if feasible, to achieve improved survival rates. Studies found patients that underwent resection of localized disease had median survival of 101 months for Stage 1 and Stage 2 tumors[45].

Discussion: Patients should be prioritized in surgical treatment of adrenal cancer (Table 1).

Testicular Cancer

Testicular cancer primarily affects younger men and any issues with management can have lasting effects. Any significant delay (4-6 months) in diagnosis of testicular cancer increased the probability of metastatic disease - 20% of patients with a delay <30 days had metastasis compared to 55% of patients with a delay >4-months[46].

After diagnosis, patients with clinical stage I or clinical stage II would need to consider management options, including primary retroperitoneal lymph node dissection (P-RPLND). For Stage I tumors, surveillance is a feasible choice during the pandemic, even for patients with high risk features [47]. Similarly, patients with Stage II tumors that may be amenable to RPLND will need to be counseled, and their final decision on surgery may depend on person preferences and hospital resources. Furthermore, chemotherapy may cause immediate side effects such as nausea, vomiting, nephrotoxicity but also lasting issues such as hypogonadism, infertility, pulmonary toxicity, cardiovascular disease, secondary malignancies, and neuropathy[48]. In reviewing the literature, the topic of delaying post-chemotherapy retroperitoneal lymph node dissection is lacking.

Discussion: Based on this data, patients with testicular cancer would likely benefit with minimized delays and diagnosis with orchiectomy should try to be prioritized. Whether patients choose chemotherapy, surgery, or surveillance for Stage II disease should be a multidisciplinary approach (Table 1).

Penile Cancer

Even outside of a pandemic, current literature describes that patients with penile cancer may experience delays in receiving medical care. In one study by Gao et al. of 254 patients, the average delay from initial symptoms to initial consultation was 116 days (SD=17.2)[49]. Patients that had delays in care demonstrated issues with sexual function at the 3-month mark, and patients with delays of greater than 6 months had significantly worse survival outcomes. In terms of the pathological effects, patients with a 3-month delay were found to have worse surgical pathology. Chipollini et al. retrospectively reviewed patients that had delays in care from time of primary surgery to inguinal lymph node dissection (ILND)[50]. In terms of RFS, ILND within 3 months had rates of 77% at 5-year RFS compared to 37.8% for > 3-month delay. For 5-year DSS, early resection < 3 months was 64.1% compared to 39.5% for > 3 months. This was further subdivided based on aggressiveness of disease. In patients with cN0 disease, 5-year DSS was 78.6% for patients that had undergone resection in < 3 months and 45.8% for patients undergoing ILND > 3 months. Patients with more aggressive disease (cN+) 5-year DSS was 31.8% (< 3 months) compared to 35.3% (> 3 months).

Discussion: Since many penile cancer patients already experience delay for initial consultation, early surgical care is important for these patients to optimize both sexual function and survival outcomes with resectable disease (Table 1).

Conclusion

COVID-19 has significantly altered the management of urologic cancers. With the possibility of another surge with COVID-19, critical analysis of the literature on surgical delay can guide timing of treatment to minimize risk to the patient and hospital resources.

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Table 1. Recommendations on urologic cancer from review of literature during the COVID-19 pandemic

Urologic Cancer	**Recommendation**
Bladder Cancer	MIBC: Minimize delay to surgery especially high risk and variant histology. Neoadjuvant therapy should be considered. NMBIC: Appropriately counsel patients on intravesical therapy based on risk of disease. Delay in TURBT can lead to worse prognosis, especially in higher risk cases. Early imaging and screening cystoscopy are important to identify burden of disease.
Renal Cancer	T1a: patients can be followed with active surveillance T1b: delaying surgical intervention is appropriate ≥T2: consider urgent surgery if patients have unfavorable pre-operative characteristics on imaging or biopsy. Locally Advanced/Metastatic RCC: Systemic therapy may benefit and allow safe surgical delay. This may also help identify patients that would benefit most from cytoreductive nephrectomy. Prefer oral therapy rather than IV/immune checkpoint inhibitors.
Prostate Cancer	Low risk prostate cancer – no significant effect with prolonged delays Higher risk prostate cancer: Likely can delay

	for several months. Can recommend neoadjuvant hormonal therapy. Risks associated with neoadjuvant chemohormonal therapy.
Penile Cancer	ILND: should undergo without significant delay from time of penectomy. Penectomy: delays can affect sexual function, can be done as outpatient.
Testis Cancer	Orchiectomy: should be done as outpatient and avoid significant delay in diagnosis Primary RPLND: other choices available depending on clinical stage. Multidisciplinary approach with urologist and oncologist. Post-chemo RPLND: should not undergo any delay.
UTUC	High risk: should undergo surgery, without delay, especially in ureter Low risk: delay should not have significant effect on surgical outcomes Thorough evaluation should be performed to assess disease burden prior to consideration of delaying secondary procedures.
Adrenal Cancer	Should undergo surgical resection, relatively poor prognosis